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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/661,558 09/15/2003 Qingbo Li 16969-053002 9049

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FISH & RICHARDSON P.C.

P.O. BOX 1022

MINNEAPOLIS, MN 55440-1022

EXAMINER

VATHYAM, SUREKHA

ART UNIT

PAPER NUMBER

1753

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
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3 MONTHS

01/03/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

10/661,558

Applicant(s)

LI ET AL.

Examiner

Surekha Vathyam

Art Unit

1753

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 September 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-19 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-19 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 15 September 2003 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 09/15/03.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____.

DETAILED ACTION

Priority

1. It is noted that this application appears to claim subject matter disclosed in prior Application No. 10/258,547, filed October 25, 2002. A reference to the prior application must be inserted as the first sentence(s) of the specification of this application or in an application data sheet (37 CFR 1.76), if applicant intends to rely on the filing date of the prior application under 35 U.S.C. 119(e), 120, 121, or 365(c). See 37 CFR 1.78(a). For benefit claims under 35 U.S.C. 120, 121, or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of all nonprovisional applications. If the application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference to the prior application must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e),

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120, 121 and 365(c). A benefit claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed benefit claim under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

If the reference to the prior application was previously submitted within the time period set forth in 37 CFR 1.78(a), but not in the first sentence(s) of the specification or an application data sheet (ADS) as required by 37 CFR 1.78(a) (e.g., if the reference was submitted in an oath or declaration or the application transmittal letter), and the information concerning the benefit claim was recognized by the Office as shown by its inclusion on the first filing receipt, the petition under 37 CFR 1.78(a) and the surcharge under 37 CFR 1.17(t) are not required. Applicant is still required to submit the reference in compliance with 37 CFR 1.78(a) by filing an amendment to the first sentence(s) of the specification or an ADS. See MPEP § 201.11.

Drawings

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2. The drawings are objected to as failing to comply with 37 CFR 1.84(p)(5) because they include the following reference character(s) not mentioned in the description: "21" (in figs. 1a and 1b) and "68" (in fig. 1b). Corrected drawing sheets in compliance with 37 CFR 1.121(d), or amendment to the specification to add the reference character(s) in the description in compliance with 37 CFR 1.121(b) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Specification

3. The disclosure is objected to because of the following informalities:

On page 3, line 33, "compolymer" should be changed to - -copolymer - -.

Appropriate correction is required.

4. Claim 6 is objected to because of the following informalities:

In claim 6, line 4, "electrophoresced" should be changed to - -electrophoresed - -.

In claim 8, line 3, "electrophoresced" should be changed to - -electrophoresed - -.

Appropriate correction is required.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1 – 2, 4 – 8 and 14 – 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Karger et al. (US 5,633,129).

Regarding claim 1, Karger ('129) discloses a method of separating a first sample comprising nucleic acids (column 2, lines 19 – 21), the method comprising: providing a matrix that is essentially free of denaturing agents (column 5, lines 50 – 52); raising a temperature of a first portion of the matrix (column 14, lines 41 – 46) to at least about 80 °C (column 13, lines 64 – 66); subjecting the nucleic acids to electrophoresis through at least the first portion of the matrix while the temperature of the first portion is at least about 80 °C (column 12, lines 49 – 67); and deliberately cooling a second portion of the matrix (column 14, lines 41 – 46) to less than about 30 °C (column 13, lines 64 – 66), the nucleic acids migrating through the second portion after they have first migrated through the first portion (column 14, lines 54 – 59).

Regarding claim 2, Karger ('129) discloses the method wherein the first portion of the matrix is raised to a temperature between 80 °C – 90 °C (column 13, lines 64 – 66).

Regarding claim 4, Karger ('129) discloses the method wherein the second portion of the matrix is cooled to less than about 25 °C (column 13, lines 64 – 66).

Regarding claim 5, Karger ('129) discloses the method wherein the matrix is completely free of denaturing agents (column 5, lines 50 – 52).

Regarding claim 6, Karger ('129) discloses the method further comprising subjecting a second sample of nucleic acids to electrophoresis within the same matrix, after the first sample has been electrophoresed (column 20, lines 18 – 22).

Regarding claim 7, Karger ('129) discloses the method comprising subjecting a total of at least 25 additional samples of nucleic acids, one at a time, without replacing the matrix (column 19, line 65 – column 20, line 1).

Regarding claim 8, Karger ('129) discloses the method wherein the temperature of at least a portion of the polymer matrix (column 14, lines 41 – 46) in which the second sample is electrophoresed is at least about 80 °C (column 13, lines 64 – 66).

Regarding claim 14, Karger ('129) discloses a method of separating a plurality of samples of biological compounds (column 23, lines 29 – 33), comprising: providing a matrix that is essentially free of denaturing agents (column 5, lines 50 – 52); subjecting a first sample to electrophoresis through said matrix (column 19, lines 61 – 65), the first sample comprising nucleic acids (column 19, lines 53 – 58), and wherein a temperature of a first portion of the matrix is sufficient to substantially denature the nucleic acids (column 19, lines 32 – 51 and fig. 8); and subjecting a second sample to electrophoresis in a separate step but through the same matrix (column 20, lines 18 – 36), the second

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sample comprising a complex of at least two biological compounds (column 19, lines 32 – 51 and column 20, lines 18 – 36).

Regarding claim 15, Karger ('129) discloses the method wherein the temperature is from about 80 °C to about 99 °C (column 13, lines 64 – 66).

Regarding claim 16, Karger ('129) discloses the method wherein the temperature is from about 80 °C to about 90 °C (column 13, lines 64 – 66).

Regarding claim 17, Karger ('129) discloses the method further comprising deliberately cooling a second portion of the matrix (column 14, lines 41 – 46) to less than about 30 °C (column 13, lines 64 – 66), the first and second samples migrating through the second portion after each has first migrated through the first portion (column 20, lines 18 – 22).

Regarding claim 18, Karger ('129) discloses the method wherein the second portion of the matrix is cooled to less than about 25 °C (column 13, lines 64 – 66).

Regarding claim 19, Karger ('129) discloses the method wherein the complex comprises at least one of a nucleic acid-protein complex and a protein-protein complex (column 23, lines 29 – 33).

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 3, 9 – 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Karger et al. (US 5,633,129) in view of Cottrell et al. (US 4,254,249).

Karger ('129) discloses the method as discussed with regards to claim 1 above. Regarding claim 3, Karger ('129) discloses the matrix comprises at least one linear copolymer comprising a first comonomer of acrylamide (column 12, lines 38 – 45).

Karger ('129) does not explicitly disclose a secondary comonomer.

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Cottrell ('249) teaches a random (column 1, lines 26 – 45), linear copolymer (column 1, lines 21 – 24) comprising a first comonomer of acrylamide and at least one secondary comonomer (column 1, lines 21 – 45).

It would have been obvious to one of ordinary skill in the art to have modified the method of Karger ('129) to include the secondary comonomer taught by Cottrell ('249) because as Cottrell ('249) explains the copolymer formed as a result has the benefit of having a high molecular weight which results in aqueous solutions having desirable viscosity with minimal amounts of the copolymer (column 3, lines 1 – 6).

Regarding claim 9, Karger ('129) discloses a method of separating a first sample comprising nucleic acids (column 2, lines 19 – 21), the method comprising: subjecting the nucleic acids to electrophoresis (column 12, lines 49 – 67) using a matrix that is essentially free of denaturants (column 5, lines 50 – 52), the matrix having at least one linear copolymer comprising a first comonomer of acrylamide (column 12, lines 38 – 45), wherein a temperature of at least a portion of the matrix (column 14, lines 41 – 46) is at least about 80 °C (column 13, lines 64 – 66).

Karger ('129) does not explicitly disclose a secondary comonomer.

Cottrell ('249) teaches a random (column 1, lines 26 – 45), linear copolymer (column 1, lines 21 – 24) comprising a first comonomer of acrylamide and at least one secondary comonomer (column 1, lines 21 – 45).

It would have been obvious to one of ordinary skill in the art to have modified the method of Karger ('129) to include the secondary comonomer taught by Cottrell ('249)

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because as Cottrell ('249) explains the copolymer formed as a result has the benefit of having a high molecular weight which results in aqueous solutions having desirable viscosity with minimal amounts of the copolymer (column 3, lines 1 – 6).

Regarding claim 10, Cottrell ('249) teaches comonomers are randomly distributed along the copolymer (column 1, lines 26 – 45), and wherein the at least one secondary comonomer is selected from the group consisting of vinyl monomers, monomers of acrylamide derivatives, monomers of acryloyl derivatives, monomers of acrylic acid derivatives, monomers of polyoxides, monomers of polysilanes, monomers of polyethers, monomers of derivatized polyethylene glycols, monomers of cellulose compounds, or mixtures thereof (column 1, lines 21 – 24), each having between 2-24 carbon atoms (see formula I).

Regarding claim 11, Cottrell ('249) teaches at least one secondary comonomer is N,N-dimethylacrylamide monomer (column 1, lines 21 – 24).

Regarding claim 12, Cottrell ('249) teaches the polymer is a copolymer polymerized using about a 1:1 ratio of acrylamide and N,N-dimethylacrylamide monomer (column 1, lines 48 – 49 and column 5, line 21 – column 6, line 55).

Regarding claim 13, Karger ('129) discloses a method of sequencing a sample comprising nucleic acids (column 6, lines 26 – 35), comprising: providing a matrix that is essentially free of denaturing agents (column 5, lines 50 – 52), the matrix having at least one linear copolymer (column 12, lines 38 – 45) comprising a buffer having a pH of at least about 8 (column 25, lines 37 – 43), a temperature of at least a portion of the matrix

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(column 14, lines 41 – 46) being at least about 80 °C (column 13, lines 64 – 66); subjecting the nucleic acids to electrophoresis through said matrix (column 12, lines 49 – 67); and prior to detecting the nucleic acids (column 14, lines 58 – 59), deliberately cooling a second portion of the matrix (column 14, lines 49 – 57) to less than about 25 °C (column 13, lines 64 – 66), the second portion of the matrix receiving nucleic acids from the heated portion of the matrix (column 14, lines 54 – 57).

Karger ('129) does not explicitly disclose the linear copolymer comprising about a 1:1 ratio of acrylamide and N,N-dimethylacrylamide monomer.

Cottrell ('249) teaches a random, linear copolymer (column 1, lines 21 – 45) comprising about a 1:1 ratio of acrylamide and N,N-dimethylacrylamide monomer (column 1, lines 48 – 49 and column 5, line 21 – column 6, line 55).

It would have been obvious to one of ordinary skill in the art to have modified the method of Karger ('129) to include in the linear copolymer a 1:1 ratio of acrylamide and N,N-dimethylacrylamide monomer taught by Cottrell ('249) because as Cottrell ('249) explains the copolymer formed as a result has the benefit of having a high molecular weight which results in aqueous solutions having desirable viscosity with minimal amounts of the copolymer (column 3, lines 1 – 6).

Double Patenting

11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct

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from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Claims 1 – 19 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 15 and 20 of U.S. Patent No. 6,926,815 in view of Karger et al. (US 5,633,129). Specifically, instant claims 1, 3, 5 – 6, 9 – 10 and 14 are rejected as unpatentable over claim 15. Instant claims 11 and 13 are rejected as unpatentable over claim 20. A one-way test for obviousness-type double patenting has been applied, as the application for US patent No. 6,926,815 was filed earlier than the instant application.

Regarding instant independent claims 1, 9, 13 and 14, claims 15 and 20 of US patent No. 6,926,815 recite all the limitations except for the explicit disclosure of the temperature of a first portion of the matrix being at least about 80 °C and a second portion of the matrix being less than 25 °C.

Karger ('129) teaches the temperature of a first portion of a matrix (column 14, lines 41 – 46) being at least about 80 °C (column 13, lines 64 – 66) and a second

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portion of a matrix (column 14, lines 41 – 46) being less than 25 °C (column 13, lines 64 – 66).

It would have been obvious to one of ordinary skill in the art to have modified the method of US patent No. 6,926,815 to include the 80 °C and 25 °C portions of the matrix as taught by Karger ('129) because it achieves the separation and detection of mutant nucleic acid sequences by separating multiple heteroduplexes from homoduplexes contained in a sample in a single assay as explained by Karger ('129) (column 14, lines 41 – 46).

Conclusion

13. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Kamahori et al. (US 5,409,586) discloses a portion of matrix at 85 °C and deliberate cooling of a second portion of matrix.

Yeung et al. (US 5,582,705) discloses using the same matrix multiple times without replacement.

Henco et al. (US 5,795,720) discloses high and low temperatures in different portions of a matrix.

Hooper et al. (US 5,885,432) discloses use of temperature responsive linear polymers used at different temperatures for electrophoretic separations.

Hammond et al. (US 6,214,187) discloses high and low temperature portions in matrix for electrophoretic separation.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Surekha Vathyam whose telephone number is 571-272-2682. The examiner can normally be reached on 7:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nam X. Nguyen can be reached on 571-272-1342. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SV
December 22, 2006



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